Dissertation on

ATTENUATION OF HEMODYNAMIC RESPONSES TO ENDOTRACHEAL INTUBATION: COMPARISON OF CLONIDINE, ESMOLOL, LIGNOCAINE AND PLACEBO.

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CERTIFICATE

This is to certify that the dissertation entitled, "**ATTENUATION OF HEMODYNAMIC RESPONSES TO ENDOTRACHEAL INTUBATION: COMPARISON OF CLONIDINE, ESMOLOL, LIGNOCAINE AND PLACEBO**" submitted by **Dr. V. MURALI MAGESH** in partial fulfilment for the award of the degree of **Doctor of Medicine in Anaesthesiology** by the Tamilnadu Dr.M.G.R. Medical University, Chennai is a bonafide record of the work done by him in the Department of Anaesthesiology, Madras Medical College, during the academic year 2007 -2010.

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CONTENTS

INTRODUCTION

The hemodynamic responses to laryngoscopy and endotracheal intubation have been recognised since 1951. The induction of anaesthesia, laryngoscopy, tracheal intubation and surgical stimulation often evoke cardiovascular responses characterised by alteration in systemic arterial blood pressure, heart rate and cardiac rhythm[1]. The response following laryngoscopy and intubation peaks at 1.2 minutes and return to baseline within 5 to 10 minutes.

Though the sympathoadrenal responses are probably of little consequence in healthy patients, it is hazardous to those patients with hypertension, coronary heart disease, cerebrovascular disease, intracranial pathology and hyperactive airways. In such cases, reflex circulatory responses such as an increase in heart rate, systemic arterial pressure and disturbances in cardiac rhythm need to be suppressed.

Prof. King et al[1]., (1951) documented myocardial ischemic changes due to reflex sympathoadrenal responses immediately following laryngoscopy and intubation with a mean increase in systolic pressure of 40mmHg even in normotensive individuals.

Pyrs Roberts et al[2]., (1971) showed exaggerated form of this response in hypertensive patients.

Various systemic as well as topical agents have been used to reduce these untoward hemodynamic responses during laryngoscopy. When compared to systemic agents, administration of local anaesthetic solutions are likely to be of limited value. The commonest strategies adopted are narcotics, vasodilators, β-blockers, calcium channel blockers, lignocaine, clonidine and other sympatholytics. In our study, we have compared lignocaine, clonidine, esmolol and placebo in suppressing stress responses to laryngoscopy and intubation.

Since clonidine, lignocaine[3] and esmolol have been known to blunt sympathetic responses to intubation , their efficacy has been compared with control (placebo) in the Department of anaesthesiology, MMC (GGH), Chennai.

AIM OF THE STUDY

For the safe conduct of anaesthesia, the hemodynamic responses to laryngoscopy and intubation should be abolished or at least attenuated to balance the myocardial oxygen supply and demand . This study was done to compare the efficacy of intravenous clonidine, esmolol, lignocaine and placebo in attenuating the hemodynamic stress responses to laryngoscopy and intubation.

PHYSIOLOGICAL AND PATHOPHYSIOLOGICAL RESPONSES TO DIRECT LARYNGOSCOPY AND INTUBATION.

Intubation of the trachea alters respiratory and cardiovascular physiology by both reflex response and by the physical presence of the endotracheal tube. Although the reflex responses are generally of short duration and of little consequence in the majority of patients, they may produce profound disturbances in patients with underlying abnormalities such as hypertension, coronary artery disease, reactive airways and intracranial pathology.

Cardiovascular responses:

The cardiovascular responses to laryngoscopy and intubation are bradycardia,tachycardia, hypertension and they are mediated by both the sympathetic and parasympathetic nervous systems. Bradycardia is often seen in infants and small children during laryngoscopy and intubation. Although rarely seen in adults, this reflex is mediated by a rise in vagal tone at the sinoatrial node and is virtually a monosynaptic response to a noxious stimulus to the airway.

The more common response to endotracheal intubation is hypertension and tachycardia mediated by sympathetic efferents via the

cardioaccelerator fibres and sympathetic chain ganglia. The polysynaptic nature of pathways from the 9^{th} and 10^{th} nerve afferents to the sympathetic nervous system in the brain stem and spinal cord results in a diffuse autonomic response which includes widespread release of norepinephrine from the adrenergic nerve terminals and adrenal medulla.

Some of the hypertensive responses to endotracheal intubation also results from activation of renin- angiotensin system with release of renin from the renal juxta glomerular apparatus and endorgan innervated by β-adrenergic nerve terminals.

The effects of endotracheal intubation on the pulmonary vasculature are probably less well understood than the responses elicited in the systemic circulation. They are often coupled with changes in airway reactivity associated with endotracheal intubation. They are:

1. reflex glottic closure , i.e. laryngospasm due to brisk motor response
2. reduction in dead space
3. increase in airway resistance
4. bronchospasm as a reflex response to intubation
5. cough efficiency is reduced.

METHODS TO ATTENUATE CIRCULATORY RESPONSES DURING LARYNGOSCOPY AND INTUBATION.

The balance of myocardial oxygen supply and demand must be preserved to minimise the risk of perioperative myocardial ischemia and infarction.

Factors affecting myocardial oxygen supply and demand

Supply:

1. heart rate – diastolic time depends upon heart rate. Hence slower the heart rate, more the diastolic time and more the oxygen supply to the myocardium.
2. coronary perfusion pressure – depends on aortic diastolic pressure and left ventricular end diastolic pressure, it increases with a high aortic diastolic pressure and a low end diastolic pressure.
3. arterial oxygen content – depends upon arterial oxygen tension and haemoglobin concentration.
4. coronary vessel diameter.

Demand :

1. basal requirement
2. heart rate
3. wall tension – preload,afterload
4. contractility.

A number of methods were used to attenuate cardiovascular response due to laryngoscopy and endotracheal intubation.

1. Deepening of general anaesthesia:

Inhalational agents – "MAC-ei" – the dose of volatile agents required to block the cardiovascular responses to endotracheal intubation. This deep level of anaesthesia achieved by inhalational agents result in profound cardiovascular depression prior to endotracheal intubation. Various agents used are halothane, isoflurane and sevoflurane.

2. Lignocaine :

a. lignocaine gargle for oropharyngeal anaesthesia.

b. aerosol for intratracheal anaesthesia

c. topical spray over vocal cords

d. regional nerve blocks – superior laryngeal nerve and glossopharyngeal nerve.

e. intravenous bolus for systemic anaesthesia.

Topical anaesthesia of upper airway has been proven to be less effective than systemic administration of lidocaine.

Mechanism :

1. by increasing the depth of anaesthesia.
2. potentiation of effects of N2O anaesthesia and reduction of MAC of volatile agents.
3. direct cardiac depression
4. peripheral vasodilatation
5. antiarrythmic properties
6. suppressed cough reflex.

3. Clonidine:

It is an alpha 2 receptor agonist. Clonidine 4 to 5 mcg/kg orally 60 to 120 minutes prior to intubation or 1 to 3 mcg/kg intravenously immediately prior to intubation attenuates hemodynamic responses. Mechanism of action of alpha 2 agonist is by decreasing central sympathetic outflow, increasing the parasympathetic tone and by decreasing circulating nor adrenaline concentration.

4. Intravenous vasodilators:

Hydralazine

Sodium nitroprusside

Nitroglycerin

5. Narcotics:

Fentanly	Morphine
Alfentanyl	Pethidine
Sufentanyl	Nalbhuphine

Fentanyl is the most commonly used narcotic agent. It is a potent analgesic, has a short duration of action, does not increase intracranial tension and has minimal circulatory changes.

6. Adrenergic blockers:

Long acting : metoprolol, phentolamine, propranolol, labetalol

Short acting: esmolol

Of these, esmolol is the most commonly used agent because of its ultrashort action.

It reduces heart rate, systolic blood pressure, ejection fraction and cardiac index but it maintains coronary perfusion pressure.

7. Calcium channel blockers:

Nifedipine, nicardipine, verapamil, diltiazem[17].

Of these agents, nicardipine has got superior action.

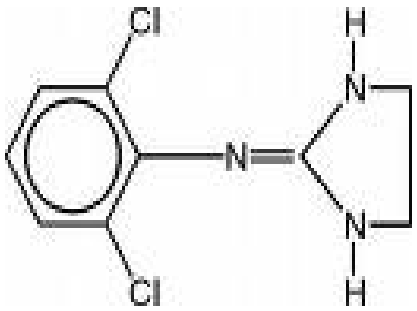
8.Sedatives and anxiolytics:

Midazolam and magnesium sulphate.

PHARMACOLOGY OF CLONIDINE

Clonidine is a prototype, partially selective alpha-2 agonist (α 2: α1 = 220:1). It is a centrally acting imidazole compound. It was synthesised in the early 1960s as a vasoconstricting nasal decongestant.

Structural formula:



Its molecular formula is (2-(2,6- dichlorophenyl amino)-2-imidazoline) and has a molecular weight of 266.56. Available as

a) 0.1mg, 0.15mg, 0.2mg, 0.3mg tablets

b) injection (parenteral) – 0.15mg/ml ampuole.

c) preservative free injection(for epidural injection) – 0.1mg/ml ampuole

d) transdermal therapeutic patch- 0.1mg/24 hrs or 0.2mg/24 hrs or 0.3mg/24hrs

Pharmacokinetics:

Oral clonidine is well absorbed with bioavailability of nearly 100%[26].Intravenously administered clonidine has a bioavailability of 100% and has a peak effect of action between 60 to 120 minutes and its action lasts for upto 8 hours. Clonidine has a low to moderate protein binding capacity (20 to 40%), mean elimintation half life of about 12 hours which is increased upto 40 hours in patients with renal dysfunction. Nearly 50% is eliminated unchanged in urine and remaining drug undergoes hepatic biotransformation. Biliary and fecal excretion is responsible for 20% of drug elimination.

Pharmacodynamics:

Clonidine acts on various systems in the body.

Cardiovascular system: Clonidine has both central and peripheral action.

Central: Activation of central α -2 adrenergic receptors in the medullary vasomotor centre inhibits the release of norepinephrine from the adrenergic neurons and reduces the sympathetic outflow from the central nervous system. Further, there is reduced discharge from the postganglionic fibres of cardiac nerves and an increase in

parasympathetic tone. This results in decrease in blood pressure, heart rate, cardiac output and peripheral venous resistance.

Nucleus tractus solitarious, the site that modulates the autonomic control including vagal activity is a important central site for the action of clonidine. Decrease in the sympathetic tone is accompanied by lowering of plasma renin activity, decrease in renal vascular resistance and maintenance of renal blood flow even when the blood pressure is lowered. Vasopressor centres of the brainstem retain their sensitivity to baroreceptor control and hence postural hypotension is considerably less than the effect of drugs that act on autonomic ganglia and peripheral adrenergic neurons.

Peripheral action: These are mediated by inhibition of norepinephrine release from the peripheral prejunctional nerve endings and by decreasing plasma concentration of norepinephrine.

Coronary circulation: The direct effect of α -2 agonists on coronary vasculature is vasoconstriction. However, this is offset by the generalised reduction in sympathetic outflow.

Central nervous system: Clonidine has sedative and anxiolytic actions. The sedative effect of clonidine may be due to decreased tonic activity of the locus coeruleus which modulates the stimuli arriving in the central nervous system. Clonidine has an opioid sparing effect and it reduces the anaesthetic requirements. It reduces the MAC value of halothane and isoflurane. It suppresses physiological and psychological symptoms after withdrawal of opioid, alcohol, benzodiazepines, barbiturates, nicotine etc., in addicted patients.

Respiratory system: It has minimal bronchodilating and respiratory depressant activity.

Endocrine system: Clonidine suppresses insulin secretion, decreases utilization of glucose by tissues and may cause hyperglycemia. It inhibits the secretion of renin.

Gastrointestinal system: It decreases salivary flow. It prevents intestinal ion and water secretion in the large bowel.

Uses:

It is used as a pre-anaesthetic medicant through oral or intravenous route and it provides sedation, anxiolysis, antisialagogue effect, decreases

doses of anaesthetic drugs, attenuates the hemodynamic responses to laryngoscopy and intubation, decreases intraoperative lability of blood pressure and heart rate, decreases MAC of volatile agents, provides analgesia and reduces post-operative shivering. Thus preservative free clonidine when injected epidurally (2-10mcg/kg) or in to the sub-arachnoid space (0.3 to 3 mcg/kg) produces dose dependent analgesia and prolongation of regional anaesthesia by acting on the substantia gelatinosa of spinal cord. Injection clonidine 3 mcg/kg administered intravenously inhibits shivering by inhibition of central thermoregulatory control. Oral clonidine attenuates the heart rate and blood pressure that usually follows ketamine administration. It is also used to diagnose phaeochromocytoma where there is lack of suppression of plasma norepinephrine to less than 500 pg/ml, three hours after a oral dose of 0.3mg clonidine. It is also used in the treatment of hypertension and diabetic diarrhoea.

Overdosage:

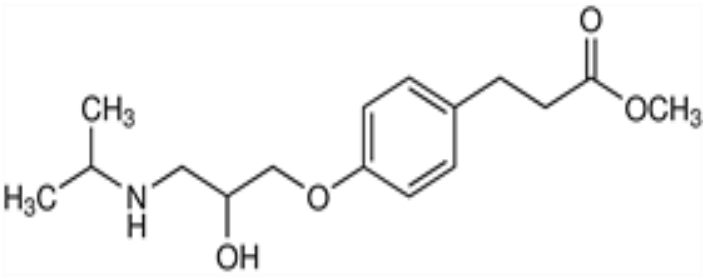
It results in depression of sensorium, transient hypertension followed by hypotension and bradycardia. It may cause respiratory depression and miosis which resembles the effects of opioid.

In case of overdosage, ventilatory support and circulatory support with crystalloids, colloids, inotropic agents and atropine are needed.

Contraindications:

Clonidine is contraindicated in patients with sinus node disease and atrioventricular node dysfunction. It is to be avoided in patients on diuretics, having hemodynamic instability and in pregnant patients.

PHARMACOLOGY OF ESMOLOL



Esmolol is a phenoxypropanolamine derivative which is structurally related to metoprolol, posses' ester group at para position of its aromatic ring. Such para substitution confers cardioselectivity on esmolol, with the ester group accounting for high metabolic lability and therefore duration of action.

Esmolol has minimal partial agonist activity and direct membrane depressant activity, but it decreases heart rate, depresses atrioventricular node conduction and decreases myocardial oxygen demand. While these actions are similar to "general" effect of beta blockers, esmolol has the clinical advantage of a short duration of action.

Cardioselectivity:

Beta blockers are classified according to their selectivity for different beta adrenoreceptor subtypes. Basically compounds active on both β-1 and β-2 receptors are non-selective. Since β-1 receptors are found mainly in the heart, drugs with greater selectivity for β-1 than β-2 receptor are cardioselective.

Electrophysiological effect:

Action of esmolol on sinus and atrioventricular node function were similar to action of other β-blockers. Significant increase in sinus cycle length, sinus node recovery time, intervals during sinus rhythm were noted. Intervals during 600ms atrial pacing and cycle length at which wenkebach periodically develop were prolonged.

Hemodynamic effects:

Reduces resting heart rate

Decreases systolic blood pressure

Left and right ventricular ejection fraction is decreased

Decreases cardiac index

These are the hemodynamic properties of esmolol in several studies involving patients with coronary artery disease and normal cardiovascular functions undergoing larnygoscopy and intubation.

Pharmacokinetics[18]:

Esmolol is rapidly hydrolysed by cytoplasmic esterases in red blood cells. It therefore has a short elimination half life of approximately 9 minutes with wide range of inter subject variability (range 6 – 15 min). Hence intravenous esmolol produces peak hemodynamic effects with in 6-10 minutes of administration.

The onset of beta blockade with esmolol shows that esmolol produces at least 90% steady state of beta blockade within 5 minutes of starting bolus dose. Only small fraction (<1%) of esmolol is excreted in urine as unchanged drug. The major fraction of intravenous dose of esmolol is detectable in urine as acid metabolites which has longer elimination half life (approximately 4 hrs) and slower clearance rate than the parent compound. However, acid metabolites has only weak β-blocking actions- approximately 1500 times less active than parent compound.

Most importantly, esmolol metabolism is not influenced by renal or hepatic functions. Drug is rapidly hydrolysed by RBC esterases and is rapidly cleared by the body.

Tolerance:

Adverse events reported during esmolol therapy include bradycardia, hypotension, deterioration of heart failure, rebound ischemia, bronchoconstriction and fatigue.

Esmolol has been rarely associated with serious cardiovascular complications like severe hypotension, cardiac arrest in patients with compensatory tachycardia secondary to hypovolemia, cardiac failure or acute myocardial infarction.

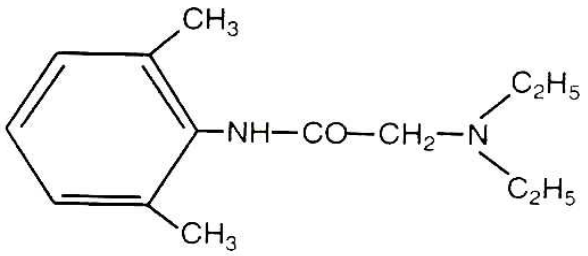
Drug interactions:

Although the onset of succinylcholine induced neuromuscular blockade was not influenced by esmolol in patients undergoing surgery with general anaesthesia, the duration of such blockade was prolonged from 5 – 18 minutes. Morphine increases the steady state blood levels of esmolol by 46%, but other pharmacokinetic parameters were not altered. Esmolol has been found to increase digoxin levels in blood by 10-20% in 12 healthy volunteers in a study. Steady state esmolol concentrations ere equivocally increased during concurrent administration of warfarin and

esmolol. Interactions between calcium channel blockers and esmolol exists and it is recommended that esmolol be used with caution in patients with left ventricular dysfunction who are receiving verapamil. Esmolol and verapamil should not be administered concomitantly in patients with conduction abnormalities and esmolol should not be given with in 48 hours of stopping verapamil treatment.

Catecholamine depleting drugs (e.g reserpine) may have additive effect when administered along with beta blockers. Thus patients receiving concurrent therapy of esmolol and catecholamine depleters, should be closely monitored for signs of bradycardia and hypotension which may lead to syncope, vertigo and postural hypotension.

PHARMACOLOGY OF LIGNOCAINE



Lignocaine is an amide local anaesthetic with antiarrhythmic properties. Lofgren first noticed that all local anaesthetics have a hydrophilic portion (secondary or tertiary amine) and a lipophilic portion (aromatic residue) separated by an intermediate chain. Linkage to the aromatic residue has provided a means for classification of local anaesthetics. Local anaesthetics with an ester linkage between the aromatic residue and intermediate chain are AMINOESTERS (procaine, chlorprocaine and tetracaine) and those with an amide linkage between the aromatic residue and intermediate chain are AMINOAMIDES (lignocaine, bupivacaine, mepivacaine etc,)

It belongs to class 1b of the Vaughan Williams classification of antiarrhythmic drugs. Lignocaine blocks the fast sodium channels in the cell membranes of myocardial cells and reduces the rate of rise of the action potential in the His purkinje system and the ventricular

musculature. The duration of the action potential and effective refractory period are reduced. The sinoatrial node and atrio-ventricular node are not affected by therapeutic concentrations of lignocaine.

Pharmacokinetics :

The pharmacokinetics of lignocaine is well described by a two compartment model following a single intravenous dose. Its distribution half life (t ½α) is around 8 minutes and its elimination half life (t½β) is around 90 to 110 minutes. Lignocaine is metabolised in the liver to monoethylglycinexylidine (MEGX) and glycinexylidine (GX) which are then excreted by the kidney. As lignocaine is rapidly cleared by the liver its plasma steady state concentration depends on the hepatic blood flow. Thus in conditions where hepatic blood flow is reduced as in congestive cardiac failure or in the presence of hepatic disease the dosage of lignocaine should be reduced. Lignocaine has a molecular weight of 234. Its protein binding is between 60-75% . Therapeutic plasma concentrations required to produce an antiarrhythmic effect is around 1.5µg/ml. Convulsions occurs at a plasma concentration of around 10µg/ml.

Indications:

1. Intravenous lignocaine is the drug of choice for management of ventricular arrhythmias like ventricular premature contractions.
2. Intravenous lignocaine is used during anaesthesia to prevent the pressor response to laryngoscopy and intubation.
3. Lignocaine is used as a local anesthetic for topical infiltration and other regional anaesthetic procedures.

It is available as 1%, 2%, 4%, and 10% solutions. A 5% solution with 7.5% dextrose is available for subarachnoid block. The preparations for intravenous use do not contain preservatives. Usual dose for intravenous administration is 1- 1.5mg/kg body weight followed by an infusion at a rate of 1-4 mg/min if required. For infiltration lignocaine can be used up to a maximum dose of 3 mg/kg body weight without adrenaline and 7mg/kg body weight with adrenaline.

Contraindications:

1. Hypersensitivity to lignocaine.
2. Hypersensitivity to other amide local anaesthetics (which is rare).

Precautions:

1. Patients with hepatic or renal dysfunction:

Lignocaine is mainly metabolised in the liver and the metabolites are excreted by the kidney. Caution should be observed while administering lignocaine to patients with these disorders especially as infusion as it may lead on to an accumulation of metabolites potentially toxicity.

2. When high doses are used in patients with impaired myocardial function it can potentiate the negative inotropic effect and cause clinical hypotension.

3. Serum potassium levels should be normalised prior to starting an infusion of lignocaine.

Toxicity:

Toxicity of local anaesthetics chiefly involves the central nervous system and cardiovascular system. The earliest symptom in an awake patient include circumoral paraesthesias and numbness, which then proceeds onto tinnitus, nystagmus and dizziness. Further increase in plasma concentration can lead onto CNS excitation restlessness and tremors leading onto convulsions. At toxic doses the combined effects of peripheral vasodilation, negative inotropic effect and a depressant action on cardiac conduction can lead onto circulatory collapse and cardiac arrest.

The ratio of the dosage or blood levels required to produce irreversible cardiovascular collapse to the dosage or blood levels required to elicit convulsions is the CC/CNS ratio. The CC/CNS ratio for lignocaine in adult non-pregnant sheep is 7 indicating that 7 times as much drug is needed to produce irreversible cardiovascular collapse as is required to produce convulsions. Hence central nervous system symptoms provide a warning in an awake patient of high plasma levels and impending cardiovascular collapse.

Management of toxicity:

1. Administer 100% oxygen , intubate if necessary.
2. seizures are managed by intravenous benzodiazepines or thiopentone sodium.
3. Cardiovascular depression is managed by intravenous fluid administration and vasopressors. Prolonged inotropic support may be required.
4. Hypoxia and acidosis worsen cardiovascular collapse and should be aggressively managed.

REVIEW OF LITERATURE

The hemodynamic consequences of endotracheal intubation have been the subject of study by various authors over many years.

Ried and Brace (1940) postulated that the reflex circulating responses to laryngoscopy and intubation were mediated through vagus nerve and named it as “VASOVAGAL REFLEXES”

King et al.,(1951) observed that a marked, through a transient rise in blood pressure which is often encountered during laryngoscopy and manipulation of the epiglottis. They stated that the impulses initiating the reflex are probably carried by the vagus nerve while the effector system is less clearly defined and may be due to decreased parasympathetic or increased sympathetic activity.

Prof.Ward and King (1960) in their study documented myocardial ischemic changes due to reflex sympathoadrenal responses following laryngoscopy and intubation with mean increase in systemic pressure of 40mmHg even in normotensive individuals.

SeinhansGanskins (1963) found that intravenous lidocaine suppressed the cough reflex, rise in blood pressure, rise in heart rate and intracranial pressure.

Masson & Eckanoff (1971) found the increase in heart rate and blood pressure are much more exaggerated in hypertensive patients which can be significantly decreased by simple lidocaine spray.

Pyrs – Roberts et al., (1971) found the increase in heart rate and blood pressure are much exaggerated in hypertensive patients.

Robert K. Stoelting et al[4]., (1977) studied about the influence of duration of laryngoscopy with or without lidocaine and found that blood pressure response was attenuated but not prevented by either oropharyngeal topical or intravenous administration of lidocaine and attempts to attenuate the response would seem to be most appropriate when intubation is likely to take more than 30 seconds.

Robert K. Stoelting et al[5]., (1978) in his study concluded that a short duration of direct laryngoscopy combined with laryngotracheal lidocaine administered just before intubation minimises pressor responses.

Robert K. Stoelting et al., (1978) demonstrated that bolus dose of sodium nitroprusside (1-2 mcg/kg) injected just before administration of induction agents was successful in attenuating the responses to endotracheal intubation.

Batra YK, Indu B, Puri GD[6] (1988) studied the attenuation of pulse rate and blood pressure responses to laryngoscopy and intubation by oral clonidine and concluded that oral clonidine does circumvent the response.

Inadae, Cullen DJ Nemeskar AR (1989)[7] compared the efficacy of lidocaine 2mg/kg, labetolol 10mg intravenous injection just prior to induction of anaesthesia and found lidocaine is a safe and cost effective mean of preventing tachycardia but not hypertension in response to laryngoscopy and intubation.

Ebert TJ Beenstien JS (1990)[8] studied the hemodynamic responses to rapid sequence induction and intubation in healthy patients with a single bolus dose of esmolol. They concluded that esmolol 2 mg/kg bolus effectively attenuated heart rate, systolic blood pressure and rate pressure product increase produced by intubation.

Sheppard S et al., (1990)[10] compared different bolus doses of esmolol and concluded that the attenuation of intubation responses is adequate following 100mg of esmolol.

Ghignone et al[21]., (1987) observed that clonidine 5 mcg/kg administered to patients with controlled hypertension was more effective in blunting the reflex tachycardia associated with laryngoscopy and intubation then lidocaine – fentanyl pretreatment.

Pouttu et al[25]., (1987) evaluated the effect of clonidine (4.5 mcg/kg) on stress responses during general anaesthesia in 21 female patients undergoing breast surgeries. They observed that clonidine attenuated the sympathoadrenal responses and the increase in heart rate and arterial blood pressure were lowered in that group.

Ghignone et al.,(1988) further studied on clonidine on intraocular pressure in elderly patients undergoing ophthalmic surgery. They observed in addition to attenuation of sympathetic responses to laryngoscopy and intubation, rise in intraocular pressure was prevented.

Nishikawa et al[22]., (1991) studied the premedication with oral clonidine in a dose of 5 mc/kg and observed that it could attenuate the pressor responses associated with laryngoscopy and intubation.

Helfman SM et al[16]., (1991) compared lidocaine, esmolol, fentanyl in attenuation of hemodynamic responses to laryngoscopy and intubation. Similar study was done by Feng et al., (1996). In both the studies, they have concluded that esmolol, offered a consistent and reliable protection in attenuating tachycardia and hypertension associated with intubation.

Vucevic M et al[11]., (1992) studied about the line of esmolol for management of cardiovascular stress responses to laryngoscopy and intubation and found that pressor responses to laryngoscopy was significantly less marked in patients given esmolol 2 minutes before intubation.

Chadha et al.,(1992) evaluated oral clonidine pretreatment for hemodynamic stability during craniotomy. They observed that pressor responses to laryngoscopy, intubation and skin infiltration was significantly attenuated in the clonidine group.

Ching KS et al., (1992) studied on comparison of fentanyl, esmolol and their combination for blunting the hemodynamic responses during rapid sequence intubation and they concluded that a combination of low dose fentanyl and esmolol provides an alternative to high dose fentanyl for blunting the hemodynamic responses to laryngoscopy and intubation.

Yuan L, chia YY (1994) studied the efficacy of bolus dose of esmolol in blunting the stress responses to intubation, comparing 100mg esmolos vs 200mg esmolol. They concluded that both bolus doses could effectively attenuate the tachycardia and hypertension produced by laryngoscopy and intubation. Further, esmolol 100mg presents a better hemodynamic stability than esmolol 200 mg during induction of anaesthesia.

Dorman et al., (1993) observed that clonidine 5 mcg/kg improves perioperative myocardial ischemia in patients undergoing CABG. Yin et al., (2002) observed the same results in CAD patients undergoing non-cardiac surgery.

Stuhmeier et al., (1996) studied the effect of small dose of clonidine (2mcg/kg) in patients undergoing vascular surgery and observed that it reduces the incidence of myocardial ischemia.

Thomson et al., (1998) compared clonidine with conventional pre-anaesthetic medication (morphine with scopolamine or lorazepam) in patients undergoing CABG and observed that clonidine produces sedation, relieves anxiety as effective as conventional premedicant. They also observed that clonidine significantly reduces the isoflurane requirements.

Tetsu kimura et al., (1998) observed that premedicant with oral clonidine (5 mcg/kg) attenuated the initial increase in heart rate without subsequent decrease in heart rate after intravenous neostigmine and atropine administration.

Groundman et al., (1997) observed that intraoperative administration of 2 mcg/kg of intravenous clonidine is suitable for prevention of postanaesthetic shivering without prolonging the recovery time.

Michael A Campagni et al., (1999) evaluated oral clondine and intravenous esmolol regarding hemodynamic changes associated with injection of epinephrine containing local anaethetic drug during endoscopic sinus surgery on septoplasty surgery in young healthy non

smokers. They observed that tablet clonidine 0.2 to 0.4 mg was efficient in blunting the hemodynamic responses.

Laurito et al., (1991)[24] concluded that oral clonidine 0.2 mg was effective in blunting systemic hypertension produced by prolonged laryngoscopy.

Bensky KP et al., (2000) in their study concluded that small doses of esmolol may block the rise in heart rate and blood pressure resulting from laryngoscopy and intubation.

Eva Oddby-Muhrbeck et al., (2002) observed that co-induction with clonidine significantly increased the number of PONV free patients after breast surgery with general anaesthesia.

Singh H [31]et al., (1995) in their study concluded that lidocaine 1.5 mg/kg intravenously and nitroglycerin 2 mcg/kg intravenously were ineffective in controlling the acute hemodynamic responses following laryngoscopy and intubation. Esmolol 1.4 mg/kg intravenously was more effective than either lidocaine or nitroglycerin in controlling stress responses.

Miller DR et al., (1991) in their Canadian multicenter trail involving five hundred and forty eight patients concluded that 100mg bolus of esmolol is a safe and effective agent. This dose of esmolol combined with a low dose of narcotic (fentanyl 2 mcg/kg) results in effective control of both heart rate and blood pressure, while avoiding important side effects.

Dipak L Raval et al[35]., (2002) compared oral clonidine and oral diazepam and concluded that clonidine was more effective in blunting sympathoadrenal responses.

Zulandaro et al[34]., (2001) compared intravenous clonidine 3mcg/kg with intravenous esmolol 2mg/kg in randomly allocated 44 patients (22 in each group) and concluded that clonidine is effective in attenuating sympathoadrenal responses to intubation than esmolol with statistical significance, p value being less than 0.05.

Carabine et al[23]., (1991) compared two doses of intravenous clonidine (0.625 mcg/kg and 1.25 mcg/kg) in attenuating intubation responses and observed that both the doses equally and effectively blunted the pressor responses to laryngoscopy and intubation.

MATERIALS AND METHODS

One hundred and twenty patients of ASA physical status 1 or 2 undergoing elective surgical procedure under general anaesthesia with endotracheal intubation were included in this study.

Patients belonging to age group 15 to 60 years of both the sexes were included. It is a prospective randomized controlled study. The study was approved by our institution ethical committee and after obtaining written, informed consent from the patient, this study was conducted.

The study was done during the period from June 2009 to august 2009 in the Department of Anaesthesiology, Govt. General hospital, Chennai 3.

Inclusion criteria:

1) ASA 1 or 2
2) Patients with airway with modified mallampatti grade class 1 or 2
3) Age group 15 to 60 years of both sexes.

Exclusion criteria:

1) Patients with full stomach
2) Patients posted for emergency surgery
3) Patients with difficult airway
4) Hypertension, diabetes, ischemic heart disease and pregnancy
5) Patients with contraindications to study drugs.
6) Patient refusal

Materials:

1) Injection thiopentone 2.5% solution
2) Injection suxamethonium
3) Injection glycopyrollate
4) Injection fentanyl
5) Injection esmolol hydrochloride(esocard) 100mg/10ml vial
6) Injection ligocaine 2% (preservative free)
7) Injection clonidine 0.15mg/ml ampoule
8) Normal saline
9) Disposable 10 ml syringe
10) Larynyngoscope with blades 3 and 4
11) Endotracheal tubes of various sizes.

Pre anaesthetic preparations:

All the patients were admitted and they underwent routine investigations like:

Hemogram

Blood urea and sugar

Serum creatinine and electrolytes

Chest x ray

Electrocardiogram

Other investigations were obtained on the basis of the condition of the patient.

Anaesthetic protocol:

Pre-operative visit was done to allay anxiety and good rapport was established with the patients. All the patients were given pre-operative night sedation with tab.diazepam 10mg orally.

Interventions:

Induction of anasesthesia was standardised for all patients. Monitors used were NIBP, ECG, Et co2 and pulse oximetry.

Method:

One hundred and twenty patients of both the sexes of ASA 1 or 2 undergoing surgical procedure were randomly allocated into four groups.

Group C (clonidine 2 mcg/kg) – 30 patients were given intravenous clonidine 2 mcg/kg 2 minutes before induction.

Group E (esmolol 1mg/kg) -- 30 patients were given intravenous clonidine 1 mg/kg 2 minutes before induction.

Group L (lignocaine 1.5mg/kg) – 30 patients were given intravenous lignocaine 1.5mg/kg 2 minutes before induction

Group P (placebo- normal saline) –30 patients were given normal saline 2 minutes before induction.

Premedication:

Patients are shifted to the operating table. Their pulse rate, blood pressure and sp02 were recorded. They were premedicated with injection glycopyrollate 4 mcg/kg body weight intravenously and injection fentanyl 2mcg/kg body weight intravenously. Then, their heart rate, blood pressure and sp02 were recorded.

Preoxygenation:

It is done with 100% oxygen for 3 minutes.

Administration of study drug:

The study drug was taken in a 10 ml syringe in a diluted form and given in bolus over 10 to 15 seconds. Then vital signs were recorded. Two minutes later, patient was induced with injection thiopentone 2.5% 5mg/kg body weight intravenously. Then, injection succinycholine 1.5mg/kg body weight was given. Intubation was performed by the same person for all the cases with appropriate sized endotracheal tubes orotrachealy.

Anaesthesia was maintained with controlled ventilation with N2O/O2 mixture 2:1 and injection atracurium 0.5mg/kg given as initial dose. No surgical stimulation was permitted for 5 minutes after intubation.

Patients were monitored throughout the period from entering into operation theatre till recovery and in the immediate post operative period by means of automated NIBP, pulse oximetry and ECG in a multichannel monitor. ECG was monitored with particular importance to any alteration

in rhythm. All patients were extubated and were shifted to post anaesthetic care unit for a follow up for 24 hours. Results were tabulated and analysis done by 't' test. A p – value of less than 0.05 was considered as statistically significant.

OBSERVATION AND RESULTS

One hundred and twenty patients under this study were categorised into four groups. 30 in each group. They compromised both sexes in the age group 15 to 60 years. The demographic profile is as follows:

Characteristics	**Group-C**	**Group-E**	**Group-L**	**Group-P**
Age (yrs)	26.03±7.10	26.67±7.87	24.97±7.90	27.90±6.30
Sex	M-15 F-15	M-14 F-16	M-17 F-13	M-13 F-17
Weight(kgs)	49.40±7.16	52.37±8.05	50.77±6.79	52.77±7.12
Basal heart rate	90.67±16.68	97.20±14.85	89.23±15.88	87.60±7.99
Basal systolic blood pressure(mmHg)	124.00±9.45	124.80±10.77	120.47±8.04	120.37±8.67
Basal diastolic blood pressure(mmHg)	83.13±7.66	82.20±6.43	80.40±6.64	78.83±6.79
Basal mean arterial pressure(mmHg)	96.73±7.79	96.47±7.69	93.80±6.47	92.63±6.82

Age group (Years)

GROUP	N	Mean	Standard deviation	F-test
C	30	26.03	7.10	F=0.8414 P=0.4739
E	30	26.67	7.87	
L	30	24.97	7.90	
P	30	27.90	6.30	

In the group C, the mean age was 26.03±7.10 years, ranging from 16 to 41. In the group E, the mean age was 26.67±7.87 years, the range being 16 to 45. In the group L, the mean age was 24.97 ±7.90, the range being 16 to 48, and in the group P, it was 27.90±6.30, the range being 18 to 46. Thus, there is no significant difference between the four groups as their p=0.4739 (p value of significance being < 0.05)

Sex distribution

Sex	Group C	Group E	Group L	Group P	Total
Male	15	14	17	13	59
Female	15	16	13	17	61
Total	30	30	30	30	120

p = 0.7609 (p value of significance being < 0.05)

The sex difference between the four groups is equal as shown in the bar chart, the difference being insignificant (p = 0.7609)

Weight distribution (kgs)

Group	N	Mean (kgs)	Standard deviation	f-test
C	30	49.40	7.16	F=0.07
E	30	52.37	8.05	p = 0.93
L	30	50.07	6.79	
P	30	52.77	6.10	

In the group C, the mean weight was 49.40±7.16 ranging from 35 to 65 kg. In the group E, the mean weight was 52.37±8.05 ranging from 42 to 73 kg. In the group L, the mean weight was 50.07±6.79 ranging from 40 to 70 kg. In the group P, the mean weight was 52.77±6.10 ranging from 44 to 70 kg. Thus there was no significant difference between the four groups as their p value = 0.93

Baseline Hemodynamic Parameters

There was no statistically significant difference in the baseline hemodynamic parameters between the four groups.

Basal Heart rate (beats/min)

Group	N	Mean	Standard deviation	f- test
C	30	90.67	16.68	F=2.607
E	30	97.20	14.85	P =0.055
L	30	89.23	15.88	
P	30	87.60	7.99	

Basal systolic pressure (in mmHg)

Group	N	Mean	Standard deviation	f- test
C	30	124.00	9.45	F=1.877
E	30	124.80	10.77	P =0.137
L	30	120.47	8.04	
P	30	120.37	8.67	

Basal diastolic pressure (in mmHg)

Group	N	Mean	Standard deviation	f-test
C	30	83.13	7.66	F= 2.306
E	30	82.20	6.43	p= 0.080
L	30	80.40	6.64	
P	30	78.83	6.79	

Basal mean arterial pressure (in mmHg)

Group	N	Mean	Standard deviation	f-test
C	30	96.73	7.79	F= 2.337
E	30	96.47	7.69	p =0.077
L	30	93.80	6.47	
P	30	92.63	6.82	

HEART RATE CHANGES (beats / min)

Group	**C**	**E**	**L**	**P**
Base line	90.67±16.68	97.20±14.85	89.23±15.88	87.60±7.99
After premedication	86.90±11.67	96.97±12.87	92.80±10.76	83.96±9.22
After study drug	82.37±9.90	85.13±12.32	96.63±9.76	84.60±11.43
After induction	88.13±16.97	87.97±12.25	97.80±13.38	87.53±10.10
At laryngoscopy & intubation	92.80±15.88	98.67±10.40	110.90±12.94	108.57±10.87
1 min	89.83±15.16	92.73±9.27	101.87±12.79	99.17±12.06
3 min	84.73±13.79	90.90±10.20	95.87±11.35	93.73±11.99
5 min	79.70±12.90	89.40±10.26	91.03±11.72	89.87±11.50

SYSTOLIC BLOOD PRESSURE CHANGES (mmHg)

Group	C	E	L	P
Base line	124.00±9.45	124.80±10.77	120.47±8.04	120.37±8.67
After premedication	122.66±8.12	123.16±11.14	119.66±9.97	122.10±9.31
After study drug	123.06±10.13	120.10±11.97	120.63±8.98	122.10±12.18
After induction	110.77±26.90	113.53±14.27	113.07±14.14	116.63±12.13
At laryngoscopy & intubation	120.27±16.21	129.30±15.06	138.80±16.90	146.33±15.91
1 min	112.60±14.25	121.40±13.10	125.77±19.01	131.73±14.87
3 min	106.47±14.55	115.70±9.91	115.17±15.19	123.17±11.41
5 min	101.90±10.63	114.20±8.83	112.17±13.94	119.50±10.22

DIASTOLIC PRESSURE CHANGES (mmHg)

Group	C	E	L	P
Base line	83.13±7.66	82.20±6.43	80.40±6.64	78.83±6.79
After premedication	82.13±9.10	80.43±11.43	79.77±7.70	80.43±10.26
After study drug	81.73±6.29	80.00±12.73	75.30±7.70	81.33±9.69
After induction	73.73±10.36	78.07±8.69	78.00±11.62	77.50±8.89
At laryngoscopy & intubation	84.73±13.83	92.00±9.66	100.27±15.50	95.90±11.57
1 min	77.57±11.45	85.60±7.05	77.80±11.99	81.70±7.99
3 min	71.53±12.13	80.67±7.05	77.80±11.99	81.70±7.99
5 min	68.93±9.78	79.07±6.31	77.03±11.64	77.30±7.48

MEAN ARTERIAL PRESSURE CHANGES (mmHg)

Group	C	E	L	P
Base line	96.73±7.79	96.47±7.69	93.80±6.47	92.63±6.82
After premedication	94.73±9.09	94.73±8.89	93.66±12.48	94.33±10.70
After study drug	95.50±12.67	93.33±9.09	94.03±8.18	95.26±11.17
After induction	86.93±14.72	89.97±10.05	89.70±12.14	90.60±8.98
At laryngoscopy & intubation	96.50±14.23	106.0±12.19	113.0±15.71	112.93±11.95
1 min	89.30±12.07	98.00±13.69	101.1±16.81	101.70±10.03
3 min	83.20±12.62	92.27±7.79	90.30±12.62	95.53±8.25
5 min	79.97±9.73	90.73±6.67	88.73±11.97	91.40±7.42

DISCUSSION

Laryngoscopy and endotracheal intubation produces hemodynamic stress responses characterized by hypertension and tachycardia. This neuroendocrine responses can cause a variety of complications in patients with cardiac disease due to imbalance of myocardial oxygen supply and demand like ischemic changes, ventricular arrythmias and cardiac failure.

This is also hazardous in patients with vascular pathologies due to weakening of lining of major arteries in particular cerebral and aortic aneurysms. In patients with hydrocephalus or intracranial mass lesions the increase in CSF pressure may produce transient impairment of cerebral perfusion leading to cerebral ischemia .

These reflex responses may be diminished or modified locally or centrally and attempts have been made to accomplish this with varying success by different techniques and agents. No effective drug has been found out so far to abolish this response totally.

Many drugs have been reported to have beneficial effects in partially attenuating sympathoadrenal responses to endotracheal intubation. Injection lidocaine, esmolol, fentanyl, calcium channel blockers have been extensively studied by many authors. Alpha 2 agonist clonidine, though not extensively studied like other drugs, there are many reports stating its beneficial effects in attenuation of circulatory responses to endotracheal intubation.

Batra YK, Indu B, Puri GD et al., in 1988 studied the attenuation of circualatory responses to laryngoscopy and intubation by oral clonidine (5 mcg/kg) and concluded that oral clonidine does circumvent the response. This study result added more supports to earlier studies conducted by Ghignone et al., and Pouttu et al in 1987. Carabine et al compared different doses of intravenous clonidine in attenuating intubating responses in 1991. Zalunardo et al compared intravenous clonidine with intravenous esmolol in attenuating intubation responses and found out that intravenous clonidine (3 mcg/kg i.v)was statistically significant (p value < 0.05) in attenuating intuabation responses when compared to intravenous esmolol (2mg/kg i.v).

Various studies have reported that lignocaine is effective[12] in blunting these responses. Recent studies, however, have questioned lignocaine's efficacy. In Singh et al's[31] , van den Berg et al's[32] and Kindler et al's[33] study IV Lignocaine 1.5 mg/kg was ineffective in controlling the acute hemodynamic response following laryngoscopy and intubation. In two different studies, it was shown that lignocaine 1.5 and 2 mg/kg is ineffective in blunting the responses during rapid sequence induction. Bachofen studied blood pressure responses to endotracheal intubation with 1.5 mg/kg lignocaine in patients with intracranial vessel malformations or brain tumors. In both groups no significant effect of lignocaine on the pressure response could be observed.

In our study , comparison of intravenous clonidine (2mcg/kg), lidocaine (1.5mg/kg), esmolol (1 mg/kg) and placebo was done in attenuating circulatory responses to endotracheal intubation. The data was analysed using Microsoft Excel, and SPSS 10.0 for windows. Haemodynamic variables were represented by mean ± SD. Statistical significance in mean difference was assessed by the use of One way analysis of variance. Tukey's HSD was applied to evaluate inter group comparisons. A p value of $< .05$ was considered as statistically significant.

Heart rate changes

The baseline mean heart rate of all the four groups did not have any statistically significant differences as their p value was 0.055. At the time of induction also there was no significant difference in mean heart rate among the four groups(p = 0.080). Once endotracheal intubation was performed, there was a rise in heart rate in all four groups, of which the rise in heart rate in group C was found to be least when compared to other groups. Though the rise in heart rate in group C is lowest, it is statistically insignificant when compared to group E (p value = 0.068). Group C and E differed from group L and P with statististical significance (p value = 0.001) in tachycardic response to endotracheal intubation. Our study results with regard to heart rate matches with Vucevic et al which proved efficacy of esmolol and Carabine et al which proved the efficacy of clonidine. Inefficiency of lidocaine in attenuating rise in heart rate in our study can be explained by comparing it with Singh et al, Van der begh et al and Kindlers et al all of whom questioned lidocaine's efficacy. The heart rate in group C stayed significantly lower than all other groups even at 5 minutes after intubation (p value = 0.001), but in group E it stayed significantly lower than group L and group P till 3 minutes after intubation. After this there was no significant difference among group E,L and P which can be explained by the short duration of action of esmolol. Thus it is inferred that though clonidine and esmolol are equally

effective in blunting rise in heart rate immediately following intubation. clonidine provides a better hemodynamic stability than esmolol for a longer duration following intubation.

Systolic blood pressure changes

There was no significant difference in baseline systolic blood pressure values (p = 0.137) among the four groups. Even at induction, there was no difference in systolic blood pressure of all the groups (p = 0.650). After intubation, there was a sudden increase in systolic blood pressures in all four groups. Group C and group E differed in attenuation of pressor response to intubation from groups L and P with statistical significance (p value 0.001). Group C had aleast rise in systolic blood pressure which when compared with group E was statistically significant (p vaule 0.007). There was no difference between group L and group P (p value 0.231) Even after 5 minutes, group C differed from all other groups showing a sustained attenuation of pressor response. At 3 minutes and 5 minutes, there were no statistically significant differences in systolic blood pressure among groups E,L and P (p value 0.124). Probably due to shorter duration of action group E could not show much difference from group L and group P at 3 minutes and 5 minutes interval . Attenuation of pressor responses by group E in our study matches with studies conducted by Yuan et al, chings et al and helfman et al. The

difference between group C and group E matches with study conducted by zulandaro MP et al in 2001 which proved clonidine was more effective than esmolol in attenuating pressor response to endotracheal intubation.

Diastolic and mean arterial pressure changes

There was no significant difference in baseline diastolic blood pressure among the four groups (p = 0.087) and also in baseline mean arterial pressure (p = 0.073). During induction of anaesthesia, the groups did not show significant difference in diastolic blood pressure or mean arterial pressure. After intubation, there was a sudden increase in diastolic and mean arterial pressures in all the four groups. Group C and group E differed from groups L and P with statistical significance in rise in diastolic blood pressure(p value 0.001) as well as in rise in mean arterial pressure(p value 0.001) . Group C had least rise in diastolic blood pressure and mean arterial pressure which when compared with group E were statistically significant (p vaule being 0.006 and 0.009 respectively). There was no difference between group L and group P both in the diastolic blood pressure (p value 0.462) and mean arterial pressure (p= 0.312). Even after 5minutes, group C differed from all other groups showing a sustained attenuation of pressor response. At 3 minutes and 5 minutes, there were no statistically significant difference in both diastolic blood pressure and mean arterial pressure among groups E,L

and P (p value 0.223 and 0.412 respectively). Again probably due to shorter duration of action, group E did not show much difference from group L and group P at 3 minutes and 5 minutes interval. Attenuation of pressor responses by group E in our study matches with studies conducted by Yuan et al, Chings et al and Helfman et al. The difference between group C and group E matches with study conducted by zulandaro MP et al in 2001 which proved clonidine was more effective than esmolol in attenuating pressor response to endotracheal intubation.

Episodes of perioperative hypertension and tachycardia with its consequent ill effects on the vital organs can be a significant problem in some patients despite adequate depth of anaesthesia and analgesia. This study shows the effectiveness of clonidine in attenuating the increase in heart rate and blood pressure following endotracheal intubation , thereby minimising significantly the imbalance between myocardial demand and supply following endotracheal intubation. Clonidine is followed by esmolol which attenuates rise in heart rate to intubation as effective as clonidine, but not as effective as clonidine in attenuating rise in blood pressure to intubation.

SUMMARY

This prospective randomised study was designed to evaluate the efficacy of intravenous clonidine, esmolol, lidocaine and placebo in suppressing the hemodynamic changes during endotracheal intubation. A total of one hundred and twenty patients belonging to ASA 1 and 2 were randomly divided into four groups. Patients in group C received clonidine 2 mcg/kg, in group E received esmolol 1 mg/kg, in group L received lidocaine 1.5 mg/kg and in group P received normal saline two minutes prior to induction.

The following observations were made:

1. Patients in group C showed the maximum attenuation of both heart rate and blood pressure following endotracheal intubation.

2. Patients in group E showed a significant attenuation of heart rate as effective as group C but attenuation of blood pressure (though effective than groups L and P) was not as effective as group C.

3. Patients in group L showed no significant difference from group P in attenuating circulatory responses and both lignocaine and placebo were ineffective.

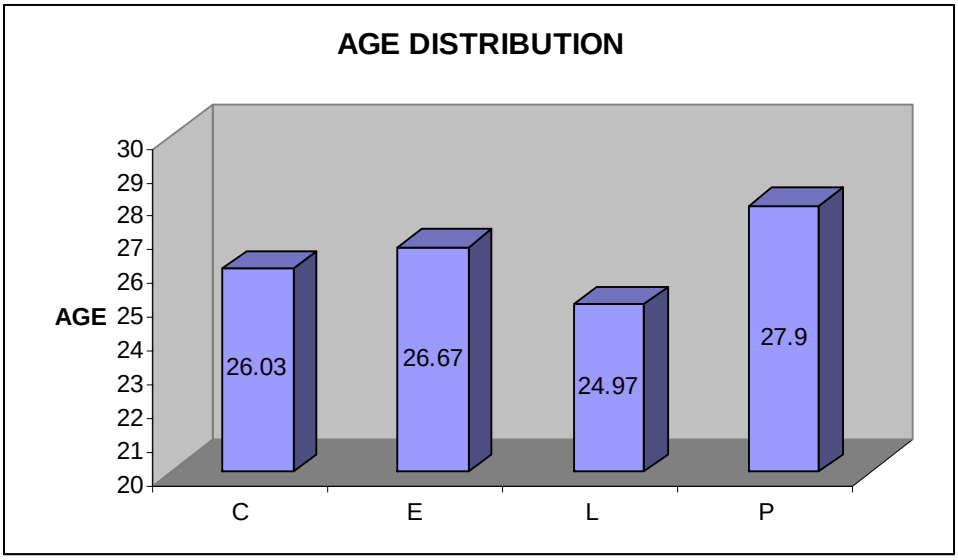
4. All the patients were recovered well from anaesthesia and none of them developed complications like severe bradycardia(HR< 50/min) or profound hypotension(SBP < 80 mmHg).

CONCLUSION

From the above study it is concluded that the hemodynamic changes associated with endotracheal intubation can be safely and effectively obtunded by using intravenous clonidine prior to induction of anaesthesia.

Clonidine is found to be effective in blunting hemodynamic responses to laryngoscopy and intubation, followed by esmolol.

Lignocaine and placebo were ineffective in attenuating these responses to laryngoscopy and endotracheal intubation.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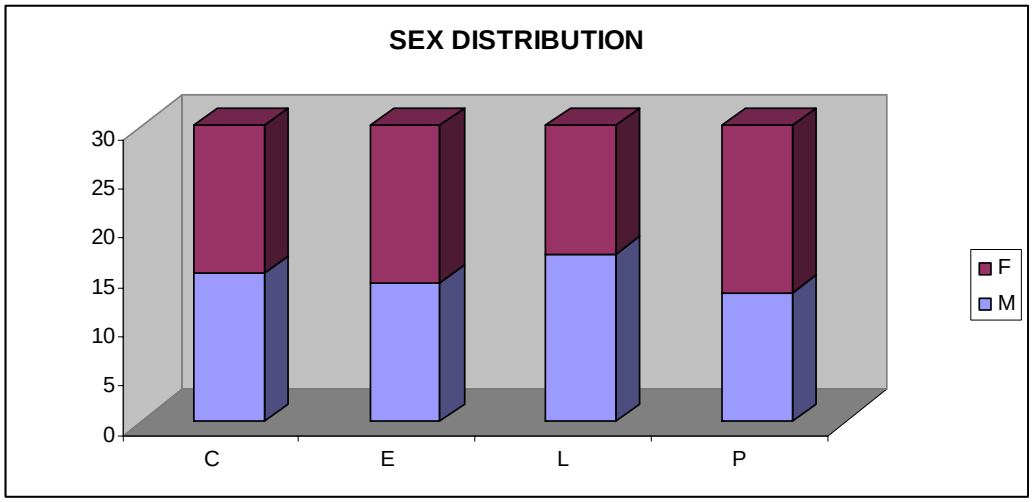
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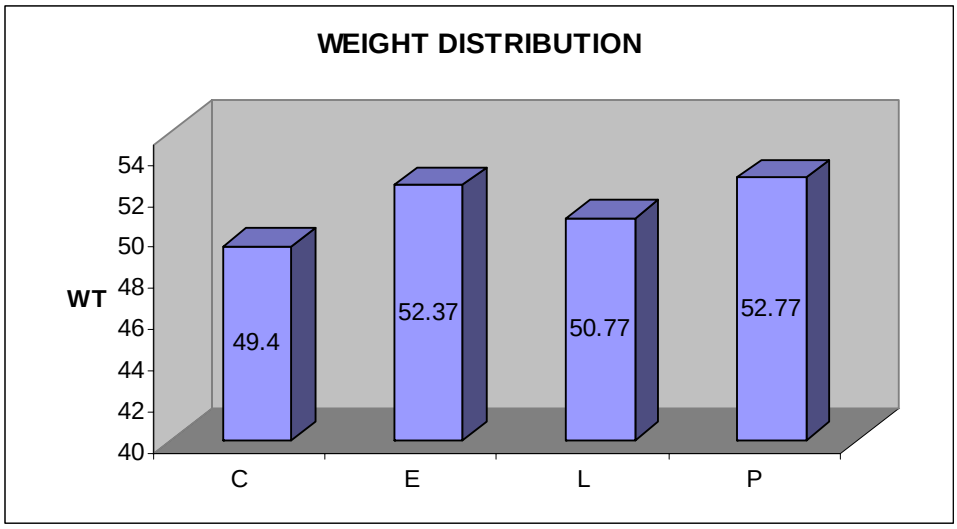
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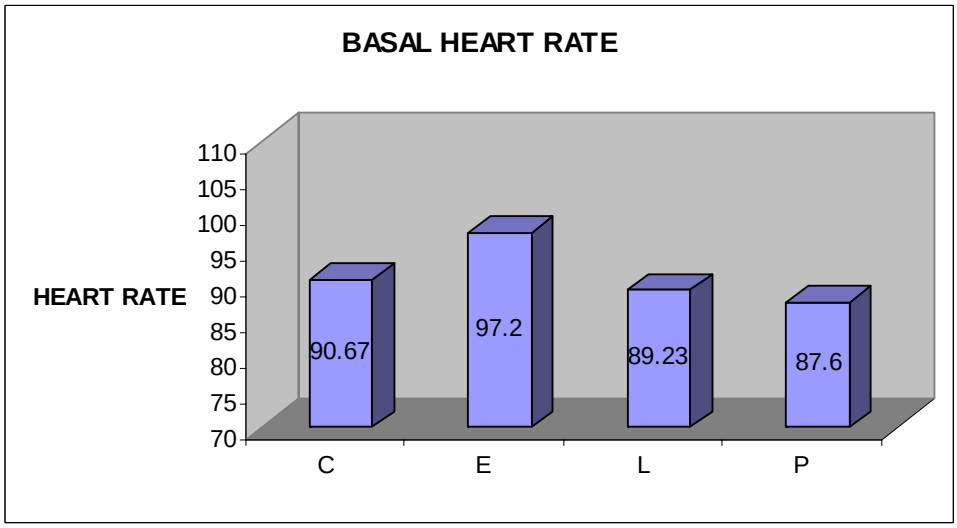
BASAL HEART RATE
HEART RATE
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85
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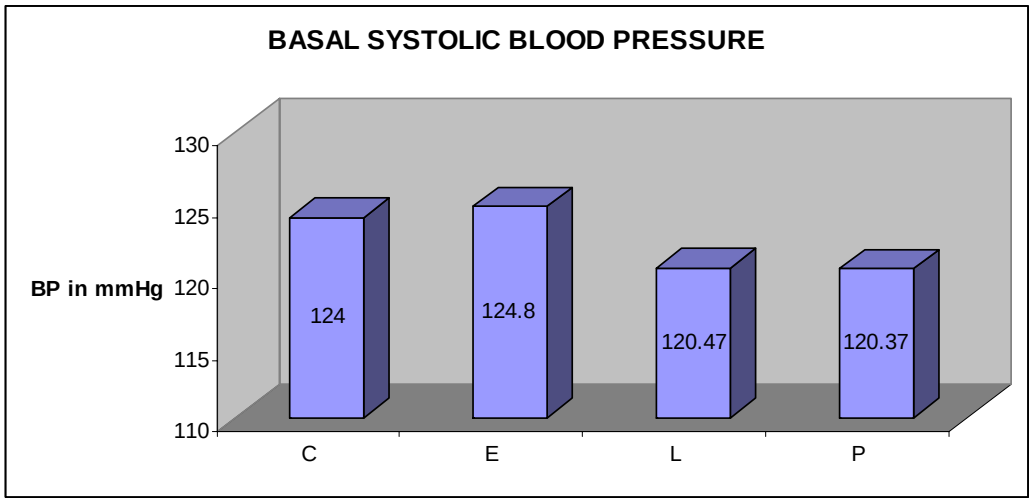
87.6
C
E
L
P


BASAL SYSTOLIC BLOOD PRESSURE
BP in mmHg
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115
110
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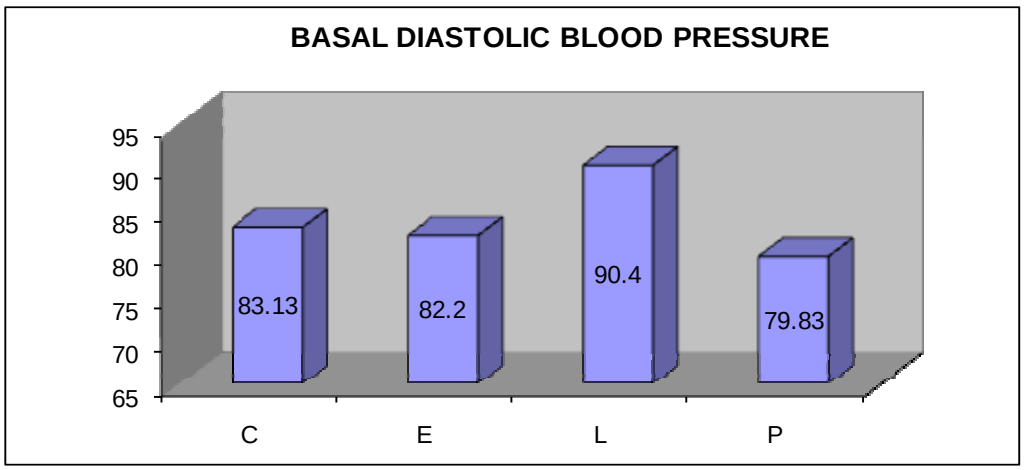
124.8
120.47
120.37
C
E
L
P


BASAL DIASTOLIC BLOOD PRESSURE
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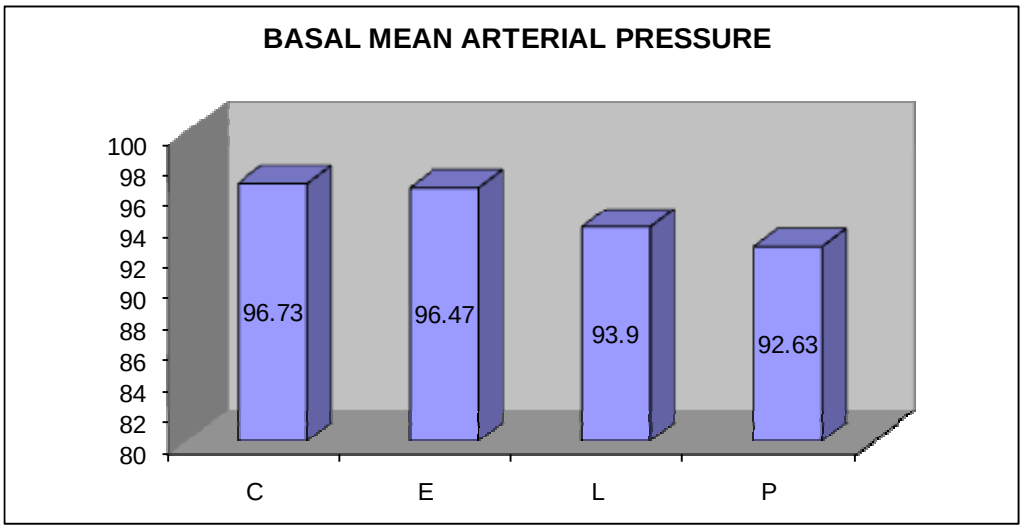
C
E
L
P


BASAL MEAN ARTERIAL PRESSURE
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C
E
L
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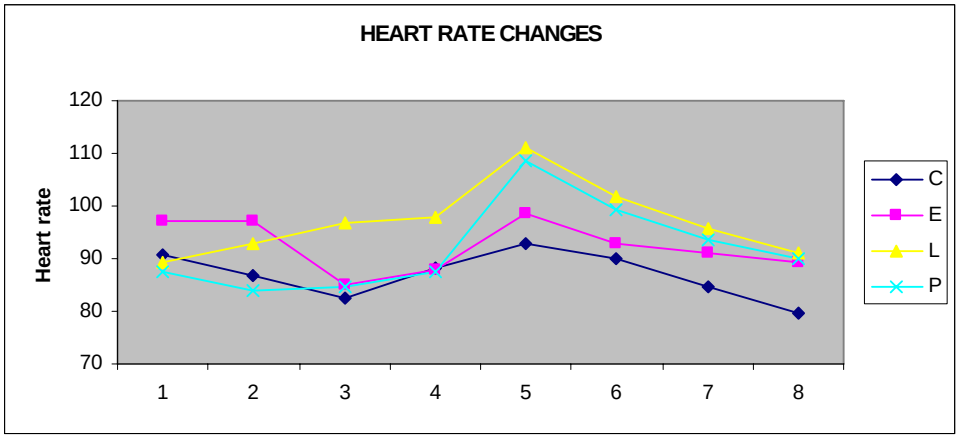
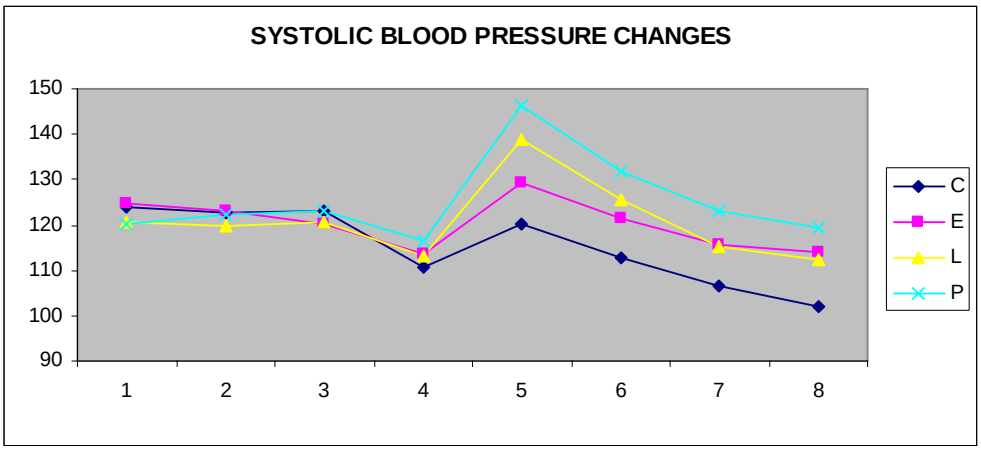
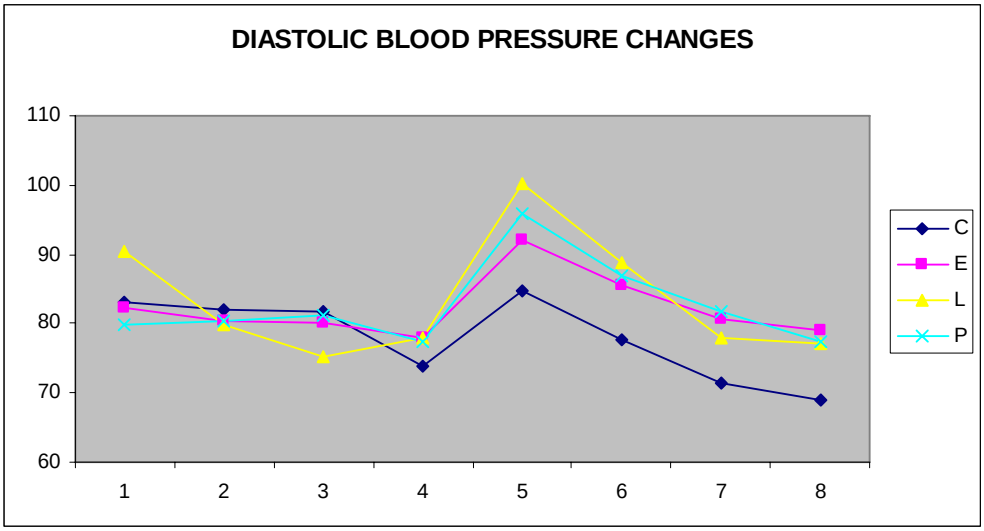


1. BASAL VALUE
2. AFTER PREMEDICATION
3. AFTER STUDY DRUG
4. AFTER INDUCTION
5. AFTER INTUBATION
6. AFTER 1- MINUTE
7. AFTER 3- MINUTES
8. AFTER 5 - MINUTES



1. BASAL VALUE
2. AFTER PREMEDICATION
3. AFTER STUDY DRUG
4. AFTER INDUCTION
5. AFTER INTUBATION
6. AFTER 1- MINUTE
7. AFTER 3- MINUTES
8. AFTER 5 - MINUTES



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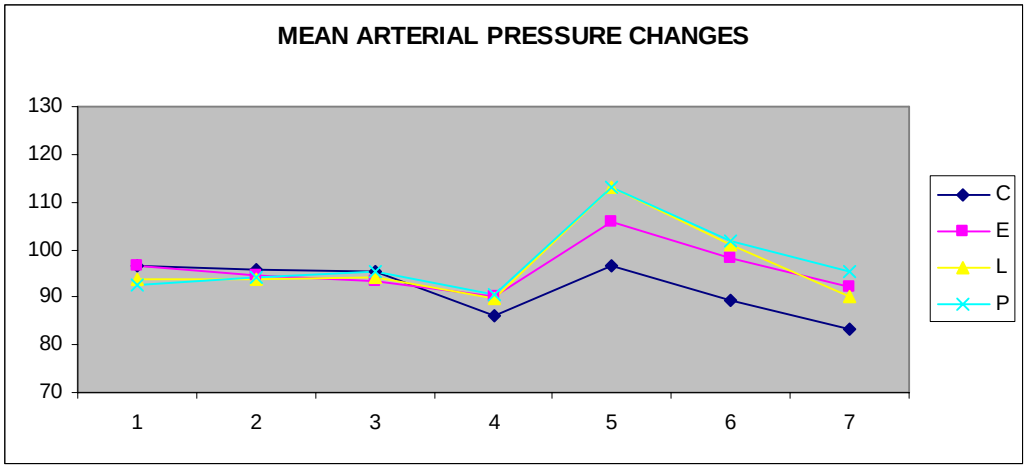

1. BASAL VALUE
2. AFTER PREMEDICATION
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6. AFTER 1- MINUTE
7. AFTER 3- MINUTES
8. AFTER 5 - MINUTES

SBP_IND	DBP_IND	MAP_IND	HR_LI	SBP_LI	DBP_LI	MAP_LI	HR_1M	SBP_1M	DBP_1M	MAP_1M	HR_3M	SBP_3M	DBP_3M	MAP_3M	HR_5M	SBP_5M	DBP_5M	MAP_5M
107	88	94	121	137	96	110	114	110	83	92	107	111	78	89	107	110	79	89
122	90	101	125	150	112	125	120	110	79	89	118	109	81	90	124	106	78	87
139	76	97	102	180	112	135	95	160	104	123	80	119	77	91	79	120	82	95
100	69	79	114	134	90	105	108	128	82	97	91	109	74	86	85	105	69	81
130	93	105	110	159	105	123	110	140	82	101	104	136	98	111	94	130	91	104
136	92	107	119	160	120	133	93	133	110	118	90	130	98	109	92	128	82	97
130	86	101	98	159	99	119	86	146	96	113	77	138	86	103	79	132	89	103
114	70	85	84	139	82	101	80	126	76	93	76	118	78	91	75	118	74	89
106	80	89	109	136	96	109	100	120	84	96	96	118	70	86	92	120	64	83
116	80	92	110	154	100	118	106	150	96	114	100	138	86	103	98	136	84	101
138	86	103	102	166	96	119	90	154	90	111	86	140	82	101	77	140	77	98
124	70	88	116	160	90	113	110	150	84	106	108	130	80	97	90	120	76	91
120	80	93	98	152	98	116	82	132	80	97	80	126	74	91	80	120	70	87
124	88	100	118	140	108	119	106	132	102	112	106	128	98	108	98	126	98	107
122	71	88	98	180	100	127	90	160	90	113	86	140	80	100	84	130	76	94
102	63	76	121	156	111	126	107	126	89	101	89	111	75	87	85	110	72	85
108	72	84	108	130	96	107	104	128	94	105	101	128	94	105	99	115	80	92
98	63	75	129	127	74	92	120	118	76	90	118	104	80	88	116	108	70	83
102	72	82	112	150	89	109	100	140	82	101	92	132	88	103	88	136	81	99
139	90	106	94	165	110	128	71	136	96	109	70	130	86	101	69	124	79	94
110	72	85	102	139	96	110	96	130	91	104	89	129	82	98	87	120	81	94
105	72	83	112	114	74	87	89	106	75	85	86	105	73	84	82	104	69	81
121	70	87	114	150	88	109	112	148	88	108	106	132	82	99	92	121	80	94
114	69	84	111	136	101	119	107	126	91	103	103	125	88	100	90	118	76	90
100	71	81	111	144	94	111	89	118	72	87	86	105	71	82	89	108	69	82
118	76	90	109	141	91	108	100	132	87	102	96	111	79	90	94	110	77	88
118	82	94	112	144	102	116	103	140	94	109	99	132	88	103	94	129	82	98
112	77	89	112	139	89	106	105	111	77	88	96	123	77	92	89	110	67	81
110	69	83	105	118	79	92	100	116	79	91	94	110	70	83	88	107	69	82
114	88	97	81	131	79	96	82	126	76	93	82	128	78	95	80	124	78	93

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PROFORMA

Drugs for obtunding intubation response

Name: Age: Sex: Wt:

ASA: MPC: IP No:

Diagnosis: Procedure:

Premedication: Inj.glycopyrollate 4µg/kg body wt.
Inj.fentanyl 2µ/kg body wt. 2 min before induction

Study drug: IV bolus

Induction: Inj.thiopentone 5mg/kg

Intubation: under succinylcholine 1.5mg/kg body wt. using appropriate sized ET tube.

Comparison of HR,SBP,DBP,MAP in study groups

Study drug ( )	**HR**	**SBP**	**DBP**	**MAP**	**Spo2**
Basal values					
After premedication					
After study drug					
Induction					
Laryngoscopy and Intubation					
1 minute					
3 minutes					
5 minutes					

Post operative period:

Recovery and extubation: